Pharmacotherapy Update

Lebanon VAMC Pharmacy

Spring 2012

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Special points of interest:

- Disease state review: Lyme disease
- Drug Information Center: sunburns, insect bites, poison ivy, oak and sumac
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- Patient Safety Notices: Statins and citalopram

Editor Notes

By: Lindsay Baun, PharmD and Dina Norris, PharmD, BCPS

Spring into Summer!! As the recent weather has taken multiple different directions, we hope this newsletter will help set you in the right direction towards the much anticipated SUMMER! In this newsletter you will find important prescribing information regarding Omega-3 Fatty Acid supplements, new FDA warnings with citalopram, updates on the new Hep C medication Boceprevir and label changes to statin medications. Have you heard of the new formulation of zolpidem, as a sublingual tablet? Not to worry because this newsletter has a great literature review of sublingual zolpidem! There are also two exciting articles regarding Lyme Disease and how to treat and prevent sunburns, insect bites, poison ivy, poison oak and poison sumac. Don't miss the favorite part of the newsletter, the Pharmacy Phun Phacts section that wraps up this edition. We hope you enjoy the most up-to-date edition of the Pharmacotherapy Newsletter and have a safe and pleasant Summer!

Would You Like a Lyme With That?

By: Lou Portas, PharmD, BCPS

After returning from a walk in the local park, you notice a small, black dot on your leg. It looks like a mole, is about the size of a poppy seed, and then you realize that it is moving! You think to yourself, *Ixodes scapularis*! *Ixodes scapularis* is the scientific name for the black legged tick (also known as the deer tick) and is one of the vectors of lyme disease transmission in Pennsylvania. Understanding the life cycle of the tick is essential to understanding how disease transmission occurs.

Lyme disease, which obtained its name from Lyme, Connecticut, is caused by a bacteria, *Borrelia burgdorferi*.[1,2] This bacteria is shaped like a corkscrew and is classified as a spirochete. Transmission occurs through the bite of an infected tick. Tick larvae hatch from eggs in the spring and feed on a host (small mammals such as mice) where they become infected with the bacteria. In the summer, larvae turn into nymphs. The winter passes and the following summer the nymphs will seek a second blood meal. This is when infections in humans will typically occur. To round out the life cycle, the adult ticks will feed on larger mammals in the summer and lay eggs the following spring.

According to the Centers for Disease Control (CDC), Pennsylvania had the second highest number of confirmed lyme disease cases in the United States in 2010, registering 3,298 cases.[2] New Jersey led the nation with the number of confirmed cases at 3,320. This disease has a high incidence in Pennsylvania and can be quite debilitating. Symptoms of Lyme disease can present anywhere from flu-like symptoms, joint pain, or effects on the heart (heart block) and central nervous system (facial nerve palsy, headaches, stiff neck, etc.). The classic sign of Lyme disease is the erythema migrans rash, also known as the "bulls-eye" rash, although it is not present in all cases. The rash tends to have concentric circles with a light colored center, is painless, and does not itch. The disease is treatable, especially if caught in the early stages. However, as the age old adage goes, an ounce of prevention is worth a pound of cure.

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Appropriate Use of Omega-3 Fatty Acid Supplements

By: Dina Norris, PharmD, BCPS

In September 2011, the Lebanon VA Medical Center P&T committee decided to simplify the ordering process for OTC omega-3 fatty acids (OTC version) due to a FDA decision making the use of combination simvastatin (at all doses) and gemfibrozil contraindicated. This decision left providers with few formulary options available to lower triglycerides in patients already on a statin medication. Currently, a provider no longer has to enter a non-formulary request for the use of these supplements. Please review the bullet points below for additional information regarding treating triglycerides and omega-3 fatty acid supplements.

Provider Clinical Points:

1. The 2004 Update to the 2001 NCEP guidelines offers the following guidelines for treating triglycerides. Triglycerides should become the primary target of lipid lowering therapy if levels are >500 due to acute risks of developing pancreatitis, otherwise, the target of lipid lowering therapy is getting the LDL to goal. In other cases, the treatment of elevated triglycerides should be made on a case by case basis due to lack of health outcomes associated with this treatment as well as potential risks due to combination therapies in particular statin-fibrate or statin-niacin combinations.

2. Omega-3 fatty acid supplements are not effective in lowering LDL levels and have no data to support this use.

3. The target dose of omega-3 fatty acid supplements to treat triglycerides is 2-4 grams of DHA/EPA per day. The dose of omega-3 fatty acids are calculated by adding the EPA+DHA amounts in each capsule.

4. You should start with no less than 4 capsules per day in order to effectively lower triglycerides . This can be dosed at 4 grams once daily or 2 grams BID.

5. There is not clinical efficacy data using doses >3-4 grams/day of omega-3 fatty acids and thus the maximum dose should not exceed 8 capsules per day.

6. Lovaza© (omega-3 ethyl esters) remains non-formulary. Omega-3 fatty acid OTC supplements should be trialed at a target dose of at least 4 capsules per day before considering a non-formulary request unless there are additional clinical situations to consider. Prior to the use of this non-formulary agent, an adequate trial of at least 4 capsules of OTC omega-3 fatty acids per day for a minimum of 4-8 weeks must be given.

7. VA PBM recommends that prior to adding a fibrate to a statin, consideration must be given to using other less toxic agents such as omega-3 fatty acids or sustained release niacin. However, like statin-fibrate combinations there is a lack of health outcome evidence demonstrating that combination therapy has benefits over statin therapy alone (Statin-fibrate safety report accessed from http://vaww.national.cmop.va.gov/PBM/Clinical%20Guidance/Forms/AllItems.aspx?RootFolder=%2fPBM%2fClinical%20Guidance%2fClinical%20Recommendations&FolderCTID=&View=%7b786029AE%2d74D9%2d40BC%2dBCC7%2dBECF18B1B7FD%7d on 9/12/11).

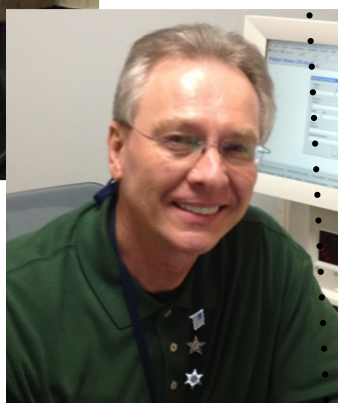
Other clinical considerations

1. Consider secondary causes of high triglycerides such as excess EtOH consumption, hypothyroidism, poorly controlled diabetes, medications (such as protease inhibitors, hormone therapy, beta-blocker, etc)
2. Omega-3 fatty acids should not be used in patients allergic to fish and/or shellfish since the EPA/DHA components are obtained from several fish sources.

References:

- Fish Consumption, Fish Oil, Omega-3 Fatty Acids, and Cardiovascular Disease. AHA Scientific Statement. *Circulation.* 2002;106:2747-2757
- Jaffri, A; Hunsinger-Norris, D. Effects of Omega-3 Fatty Acids on Triglyceride Reduction: Retrospective Evaluation in a Veteran Population. *Federal Practitioner*. 2010:April: pp. 15-22.

Pharmacist Q&A Corner Featuring: Steve Harkaway



Q. What led you into the pharmacy profession?

A. As a young boy, I remember going to the local pharmacy with my mother. The pharmacist would show me the different capsules and tablets. All the unique sizes, shapes and colors grabbed my attention. He was also mixing something in a bowl, which I've come to identify as a "mortar" and "pestle." Anyway, I said to my mother, "that's what I want to be when I grow up." Fate has a funny way.

Q. Where did you graduate pharmacy school?

A. I graduated from Temple University School of Pharmacy, located in Philadelphia, PA. Later on I obtained a Master's in "Health Services Administration," from St. Francis University, located in Joliet, Illinois.

Q. What is your previous work experience prior to coming to Lebanon?

A. Prior to coming to the VA, I worked at the MS Hershey Medical Center, where I was the Supervisor of Sterile Products. I then went to Medco Containment Services, a mail order facility, where I was a staff pharmacist. Lastly, I spent a short time with Rite Aid prior to coming to the VA.

Q. What do you love most about working at LVAMC?

A. The insight and understanding I have gained about the toll war takes on America's young men. And listening to their stories from conversations in the counseling room.

Q. What do you like to do in your free time?

A. Playing my guitar, reading, exercising, and taking long walks with my wife.

Q. Has joining *Flies in December changed your life in any way?**

A. It has helped make me a better guitar player. By that I mean it has challenged me to learn other styles of music. But most importantly, "it keeps me young" and hey, "it's really a lot of fun!!!!"

**Flies in December* is a garage band

FDA Warnings with Citalopram (Celexa®)

By: Allen Ayala, PharmD, BCPP

Prior to and after its approval in the United States in 1998, there were concerns with citalopram and the prolongation of the QT Interval in overdose situations reported in case reports in the Journal of Toxicology- Clinical Toxicology (1997) and Clinical Neuropharmacology (2001). Who would have thought post-marketing reports and results from an unpublished QT study (2011) would prompt the FDA to issue a safety communication about abnormal heart rhythms associated with high doses of CELEXA®? Almost two weeks prior to the FDA announcement on August 24, 2011, Forest Laboratories released a Dear Healthcare Professional letter addressing the dose dependent QT prolongation caused by CELEXA®.

The ensuing Drug Safety Communication from the FDA states:

1. "Citalopram should no longer be used at doses greater than 40 mg/day because it could cause potentially dangerous abnormalities in the electrical activity of the heart."

Doses higher than 40 mg bestows no additional benefit

2. Citalopram is not recommended for use in patients with:
   - Congenital, long QT syndrome
   - Bradycardia
   - Hypokalemia or hypomagnesemia
   - Recent, acute myocardial infarction
   - Uncompensated heart failure
   - Other medications that can also prolong the QT interval

3. The maximum recommended dose of citalopram is 20 mg/day for:
   - Patients with hepatic impairment
   - Patients older than 60 years of age
   - Patients genetically classified as CYP450 2C19 poor metabolizers
   - Patients taking cimetidine (Tagamet®) or other CYP450 2C19 inhibitors

Exceeding the recommended 20 mg/day in this patient population, confers a higher concentration of citalopram, which is associated with a higher risk of QT interval prolongation and Torsade de Pointes.

Summertime Sufferings

By: Emily Davies, PharmD, PGY1 Pharmacy Resident

Everyone likes to enjoy the sunshine and warm weather once summer comes around. While summer is a great time for relaxation, vacation, and sun, it is also riddled with common ailments that are preventable! This article will discuss preventative measures for sunburns, insect bites, and for contact dermatitis due to poison ivy, poison oak, and poison sumac.

SUNBURNS Intense intermittent sun exposure, history of sunburns, and experiencing 2 or more painful sunburns before the age of 15 all increase the risk of melanoma. The risk for melanoma increases with the increased quantity of sunburns in the early years of life. Each year about 8,000 people in the U.S. die from melanoma with one million new cases diagnosed each year. Risk factors for sunburns include having light hair and eye color, and a high degree of freckling or body moles.

There are 3 major types of ultraviolet (UV) radiation: UVA which penetrates deeper into skin and can harm underlying tissue, damage DNA, and suppress the immune system; UVB which can cause the most skin damage and is the most powerful between 10am and 4pm; and UVC which has little effect on the skin. Sun Protection Factor (SPF) is defined as the ratio of skin protection from using sun block versus not using sun protection. SPF only measures the amount of protection from UVB rays. The SPF equates to how much time a person can be exposed to UVB rays before the first perceptible redness of sunburn (erythema) occurs. For example, a person who normally experiences erythema within 10 minutes of sun exposure can extend this time to 150 minutes with an SPF 15 sunscreen. The number of SPF is not a linear association, as SPF 15 blocks about 93% of UVB rays, compared to SPF 40 which blocks about 97.5% of UVB rays. There are two different types of sunscreens, physical blockers that reflect and scatter UV radiation, and chemical blockers that absorb UV radiation. Some physical barriers like titanium dioxide and zinc oxide can also have some chemical sun block properties.

When buying sunscreen this summer, make sure to read the labels. As of 2012, there are new labeling requirements making it easier to pick a product. Products labeled "Broad Spectrum" offer both UVA and UVB protection. Products can be labeled "Broad Spectrum" if they are an SPF 15 or greater and pass a broad spectrum test measuring a product's UVA and UVB protection. Products can no longer be labeled "waterproof," or "sweat proof," but can be labeled "water resistant," with the label stating whether they remain effective for 40 or 80 minutes when swimming and include specific reapplication directions. To apply sun screen, put on a generous amount (1 ounce) of sunscreen, 15 minutes before going outside then reapply every 2 hours, and after swimming, sweating, and toweling off.

Certain medications and classes of medications can cause photosensitivity. Medications or medication classes include, but are not limited to: NSAIDs, antibiotics, sulfonylureas, antihistamines, antifungals, antineoplastics, clopidogrel , antipsychotics, hormones, sedatives/hypnotics, vitamins, anticonvulsants, antidepressants, antiretrovirals, antivirals, cardiovascular medications including thiazides, diuretics, antihypertensives, and statins, dietary supplements, and skin agents.

INSECT BITES Not only are insect bites annoying and itchy, but mosquitoes can also carry West Nile Virus (WNV), so prevention of a bite is key. About 80% of patients who get WNV experience no symptoms, but up to 20% of infected patients will develop flu-like symptoms and one out of 150 will develop severe illness with neurologic symptoms that may be permanent. Onset of WNV symptoms typically present in three days to two weeks after being bitten by an infected mosquito.

At home, frequently change any sitting water to help prevent mosquito breeding grounds. Some easy ways to prevent mosquito bites include using screens on your windows and staying indoors during dawn and dusk when mosquitoes are most active. Using insect repellents on skin and clothing is another common way to prevent insect bites. Insect repellents containing DEET (N,N-diethyl-m-toluamide or N,N-diethyl-3-methylbenzamide) are very effective. DEET products (*Off!, Ultrathon, Cutter,* etc.) repel mosquitoes and ticks, with higher concentrations lasting longer than lower concentrations (e.g. 30% DEET lasts about 6 hours where 7% DEET lasts about 2 hours; products with more than 30% DEET will not last much longer than 6 hours). DEET products are safe for adults and children over two months old. An alternative to DEET is picaridin (*Cutter Advanced*, *Natrapel*, etc.). Picardin, in contrast to DEET, will not irritate the skin and will not damage plastic or clothing. Like DEET, higher concentrations of picaridin will last longer, with 20% picaridin recommended for adults, and 5-10% picaridin for children over six months old.

For those who want a more natural or plant based insect repellent, there is oil of lemon eucalyptus *(Repel Lemon Eucalyptus*, etc.) that repels mosquitoes and ticks and can last up to 6 hours, but is not safe for kids under the age of three. There is also soybean oil (*Bite Blocker*, etc) and citronella oil (*Buzz Away*, etc) that does not last as long as previously mentioned products. In addition to insect repellents, there are also permethrin products (*Repel Permoanone, Fite Bite, etc.)* that can be used with insect repellents for additional protection. Permethrin products are to be sprayed onto clothes and left to dry before wearing. Spraying permethrin on the skin renders the permethrin ineffective as it combines with lipids on the skin. Recommend staying away from combination sunscreen with bug repellent products. Sunscreen needs to be applied more liberally and frequently than bug repellents. If both types of products need to be used, apply sunscreen first and allow to bind to skin, and then apply bug repellent.

POISON IVY, POISON OAK, POISON SUMAC These plants are members of the *Toxicodendron* family and are the most common causes of allergic contact dermatitis. About 50% of people exposed to these plants experience dermatitis in response to the plant resin urushiol oil, and about 30% of people will react if exposed to large amounts of the plant oil.

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Update on New Hep C Medication: Boceprevir

By: Monica Bowen, PharmD, BCPS

Boceprevir is one of the recently approved protease inhibitors which is used in combination with peginterferon and ribavirin for the treatment of patients with genotype 1 hepatitis C. Along with telaprevir, these agents represent a huge step forward in the treatment of this condition as they provide a new treatment option for patients who have previously failed therapy. Boceprevir is the VA formulary protease inhibitor. Following is some important information about this new drug.

Drug interactions: Boceprevir is a strong CYP3A4 inhibitor, potential p-glycoprotein inhibitor, and also partly metabolized by CYP3A4 and p-glycoprotein, meaning that boceprevir could potentially increase/prolong the effects of other drugs in terms of therapeutic and adverse effects, and other drugs could increase or decrease exposure to boceprevir. Many interactions are theoretical based on this information, as boceprevir has not specifically been studied with many concomitant medications. Some examples of commonly used medications which are contraindicated with boceprevir include simvastatin, lovastatin, carbamazepine, phenytoin, and drospirenone. Some medications which have dose restrictions or are not recommended to be used with boceprevir include PDE-5 inhibitors, azole antifungals, nifedipine, inhaled fluticasone and inhaled budesonide.

Cost: Boceprevir is costly at $8.80 per capsule, which makes a 28-day supply just under $3,000.

Processing/dispensing: Monica Bowen and Inga Washington process all boceprevir orders. However, be aware that if you come across pending orders for a patient who is on concomitant boceprevir, all pertinent drug interactions may not fire in the VISTA system, therefore, drug interactions should be checked using a drug database before verifying the new medication(s).

Counseling Points:

- Compliance is VERY IMPORTANT to avoid resistance and subsequent treatment failure
  - Dosing is four x 200mg capsules by mouth every 8 hours with food
- After dispensing, the capsules may be stored at room temperature for 3 months.
- Missed doses:
  - If it is <2 hours before the next dose, skip the missed dose (never double your dose)
  - If it is >2 hours before the next dose, take the missed dose as soon as possible
- Take the next dose at the scheduled time
- Do not take this medication if you or your partner are pregnant or planning to become pregnant (ribavirin is category X and boceprevir is only used in combination with ribavirin/peginterferon)
- Boceprevir can decrease the effectiveness of oral contraceptives
  - Use 2 alternate forms of birth control at all times

References:

Victrelis™ [package insert]. Whitehouse Station, NJ: Merck & Co, Inc; 2012 Apr.

Boceprevir (Victrelis™). National Drug Monograph. Pharmacy Benefits Management Services and the Medical Advisory Panel, Veterans Health Administration, Department of Veterans Affairs; 2011 Jun.

Cost information: McKesson Connect [http://connect.mckesson.com]. Accessed 2012 May 1.

Cont. From Page 4: Summertime Sufferings

Contact dermatitis can result from direct contact with bruised or injured plants, indirect contact from clothing and objects that have come into contact with the plant, or via smoke from a burning plant or release of urushiol into air when plants are cut down. Dermatitis can occur within in 24-48 hours of contact and can last one to four weeks. The main signs and symptoms include red swollen papular lesions that are very itchy. The intensity of the itching is normally what causes patients to see a health care provider. The first few days the lesions may weep, but fluid from these lesions is not contagious and will not cause lesions to spread. These contact dermatitis syndromes are self limiting and rarely have lasting consequences.

Prevention is the preferred approach for poison ivy. Avoiding the plants, wearing protective clothing, and using vinyl gloves while outside gardening are all easy preventative measures. Rubber gloves will not help protect from poison ivy, as they may allow penetration of the antigen. If it is known ahead of time that contact is a risk or certainty, use of topical barriers like bentoquatam (*Ivy Block),* which is FDA approved for protection against poison ivy when applied before contact as it physically blocks urushiol from contacting the skin, is recommended. Products are to be applied 15 minutes before exposure, then every 4 hours thereafter. Other topical barriers like *Hydropel* and *Hollister Moisture Barrier* have been shown effective in preventing contact dermatitis from the *Toxicodendron* family.

Washing the skin with soap and water immediately after skin is exposed to the plants may also prevent contact dermatitis. Urushiol can bind to the skin within five minutes, and must be removed within 10 minutes to help prevent dermatitis. The physical force of the water can remove urushiol from the skin. There does not seem to be a significant difference in efficacy between the use of a surfactant agent, an oil removing compound or a chemical inactivating agent like *Tecnu.* It is important to remember to wash well under the fingernails, as this area can be a reservoir for urushiol and can induce spread of lesions. There is also the product, Zanfel, which contains ethoxylate and sodium lauryl sarcosinate, a detergent. While Zanfel is expensive, the manufacturers claim it is effective up to 144 hours, or 6 days, between exposure and symptomatic reaction.

In summary, practicing preventative measures is key to reducing the risk for these "sufferings". Reading and following labels is crucial in order for products to provide maximum benefit and knowing how to prevent these ailments can help minimize discomfort and make for a very enjoyable summer!

References:

PL Detail-Document, New Requirements for OTC Sunscreen Products. *Pharmacist's Letter/ Prescriber's Letter.* August 2011: 270808

Recommendations for the use of insect repellents. *Pharmacist's Letter/Prescriber's Letter* 2010; 26(7):260710

Management of poison ivy. *Pharmacist's Letter/Prescriber's Letter* 2005;21(7):210706

Clinical Pharmacology. Tampa, FL: Gold Standard, Inc; 2011. URL: http://cp.gsm.com http://www.clinicalpharmacology –ip.com/default.aspx.

FDA Announces Changes to Better Inform Consumers About Sunscreen 6/14/11. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm258940.htm

Sunscreen Labeling According to 2011 Final Ruling. http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM258718.pdf.

Novel FDA Indication for Sublingual Zolpidem

By: Kendra Vong, PharmD, BCPS, PGY2 Health-System Pharmacy Administration Resident

According to the National Center for Sleep Disorders Research at the National Institutes of Health, approximately 30-40% of adults have some symptoms of insomnia within a given year, and approximately 10-15% of adults have chronic insomnia. The 1995 US insomnia cost-of-illness study reported an estimated annual direct cost of insomnia for the non-institutionalized civilian population at $14 billion, of which approximately $2 billion were attributed to medication and the remainder to health care services. Similarly, based on a literature review conducted in 1993, the National Commission on Sleep Disorders Research estimated the direct cost of insomnia at $15.4 billion annually in the US. Zolpidem, a non-benzodiazepine sedative-hypnotic, is one of the most frequently prescribed hypnotic agents. It was proven as effective as benzodiazepines in the management of short-term insomnia but with fewer adverse effects. In contrast to benzodiazepines, zolpidem has a higher affinity at the α1-subunits of the γ-aminobutiric acidA (GABAA) receptors, providing the desired clinical sedation with minimal next-day effects on cognition and psychomotor performance when administered with adequate sleep time.

In 1992, zolpidem IR was the first non-benzodiazepine sedative-hypnotic approved in the US for the treatment of insomnia, targeting sleep initiation. Subsequently, zolpidem CR came on the market in 2005 for the treatment of insomnia, targeting sleep maintenance. Alternative routes of administration were later marketed with a more rapid onset of action and/or ease-of-use. These alternative formulations include oral disintegrating tablets (ODT) launched in 2007, later discontinued by the manufacturer; oral spray launched in 2008; sublingual standard dose (5, 10 mg) and low dose (1.75, 3.5 mg) launched in 2009 and 2011, respectively. Standard dose zolpidem SL was introduced with a rapid onset of action and a statistically significant improvement on the effects of sleep initiation (latency to persistent sleep, sleep onset latency, and latency to stage 1) compared to oral zolpidem. Effects on sleep maintenance, sleep architecture, subjective sleep parameters, and next-day residual effects were comparable between the two formulations. Standard dose sublingual zolpidem is indicated for short-term (e.g. <2 weeks) treatment of insomnia characterized by difficulties with sleep initiation.

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Update: Safety Label Changes to Statins

By: Heather Spoonhower, PharmD, PGY2 Ambulatory Care Resident

The FDA approved safety label changes to the statin drug class, as a whole, in February 2012 to provide the public with information for the safe and effective use of statins.

Updates include:

1. Monitoring for Liver Enzymes

- Labels have been revised to remove the need for routine periodic monitoring of liver enzymes in patients taking statins.
- Labels now recommend that testing should be performed prior to starting statin therapy and as clinically indicated thereafter.

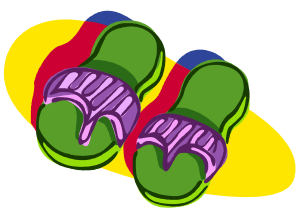
2. Adverse Event Information

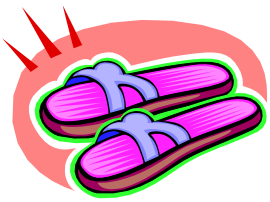
- Labels have been updated to include information about the potential for generally non-severe and reversible cognitive side effects and reports of elevations of blood sugar and HgbA1C.
- FDA states that the cardiovascular benefit of statin therapy outweighs these risks.

3. Drug Interactions

- Lovastatin labels have been updated to include new contraindications and dose limitations with certain medications that can increase risk of muscle injury when taken with lovastatin concomitantly.

Contraindicated with lovastatin:
· Itraconazole
· Ketoconazole
· Posaconazole
· Erythromycin
· Clarithromycin
· Telithromycin
· HIV protease inhibitors
· Boceprevir
· Telaprevir
· Nefazodone
Avoid with lovastatin:
· Cyclosporine
· Gemfibrozil
Do not exceed 20 mg lovastatin daily with:
· Danazol
· Diltiazem
· Verapamil
Do not exceed 40 mg lovastatin daily with:
· Amiodarone
Avoid large quantities of grapefruit juice (>1 quart daily)





Cont. from Page 6: Novel FDA Indication for Sublingual Zolpidem

Patients should have a full 7 to 8 hours of sleep before being active. Low dose sublingual zolpidem has a novel FDA approved indication for treatment of insomnia characterized by difficulty returning to sleep after middle-of-the-night (MOTN) awakening. This product has a unique gender specific dose recommendation because women were found to clear sublingual zolpidem at a slower rate than men. The recommended dose is 1.75 mg for women and 3.5 mg for men for treatment of MOTN insomnia. Dose adjustments are needed for elderly and hepatically impaired patients.

The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and the International Classification of Sleep Disorder (ICSD-II) do not have diagnostic criteria for MOTN insomnia. However, a proposed revision in DSM-5 (soon to be released) includes "difficulty maintaining sleep characterized by frequent awakenings or problems returning to sleep after awakenings" as one of the insomnia symptoms needed from the set of diagnostic criteria to make the differential diagnosis of Insomnia Disorder.

Currently, the only non-benzodiazepine sedative-hypnotic agent listed on the VA National Formulary is zolpidem IR (Ambien). The overall safety and efficacy between IR and SL formulations are similar. Standard dose zolpidem SL (Edluar®) is used for the treatment of short-term insomnia characterized by difficulties with sleep initiation. The alternative mode of delivery may be useful by those patients who have difficulty swallowing, are unable to swallow, or do not tolerate oral administration. Low dose zolpidem SL (Intermezzo®) is ideal for patients that need to take the medication as needed for the treatment of sleep maintenance insomnia characterized by prolonged wakefulness after MOTN awakenings. It is not indicated for the treatment of MOTN awakening when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking. Administering low dose zolpidem SL on an as needed basis for MOTN awakening helps to prevent unnecessary drug exposure compared to nightly prophylactic dosing.

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Staner C, Joly F, Jacquot N, et al. Sublingual zolpidem in early onset of sleep compared to oral zolpidem: polysomnographic study in patients with primary insomnia. Curr. Med. Res. Opin. 2010. 26(6):1423-1431.

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Ohayon MM, Krystal A, Roehrs TA, et al. Using difficulty resuming sleep to define nocturnal awakenings. Sleep Med. 2010;11(3):236-241.

Edluar: zolpidem tartrate sublingual tablets. Formulary Dossier. Meda Pharmaceuticals. Nov 2010.

Intermezzo: zolpidem tartrate sublingual tablet, CIV. Formulary Submission Dossier. Purdue Pharma L.P. Dec 2011.

Cont. from Page 1: Would You Like a Lyme With That?

There are several products available on the market to repel *Ixodes scapularis*. Products that contain greater than 20% DEET may be used on the skin to ward off ticks. Clothing may also be treated with permethrin products as an added form of protection. It is important to wear long pants that are a light color (tucked into boots) when walking through tall grass, however, avoiding these areas during the warm months is the best measure to decrease exposure.

Treatment of Lyme disease varies depending on the severity. The 2006 Infectious Disease Society of America (IDSA) guidelines recommend doxycycline 100 mg twice daily, cefuroxime 500 mg twice daily or amoxicillin 500 mg three times daily for early disease. Treatment duration ranges from 10-21 days.[3] Ticks also transmit other diseases, one of which is caused by a bacteria *Anaplasma phagocytophilum*. The disease caused by *A. phagocytophilum* is called Human Granulocytic Anaplasmosis (HGA). Doxycycline treats HGA but cefuroxime and amoxicillin do not. Hence doxycycline is the preferred first line agent due to the risk of co-infection with both Lyme disease and HGA. This is the proverbial "two for one"deal. If neurologic involvement is present (defined as radiculopathy or meningitis) intravenous therapy with ceftriaxone is recommended. The typical dose of ceftriaxone for this indication is 2 grams daily for 14 days. Cefotaxime and Penicillin G may be considered alternatives. There is also data to support oral doxycycline for this indication, especially in light of a beta-lactam allergy.

Knowing that we can take measures to prevent the transmission of Lyme disease should add a sense of comfort to those who will be enjoying the outdoors this summer. Remember to take all of the appropriate precautions and hopefully this summer you won't have to deal with *Ixodes scapularis*!

References:

1. www.ct.gov/dph/cwp/ . Accessed May 2012.
2. http://www.cdc.gov/lyme/. Accessed May 2012.
3. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America. CID 2006;43:1089-134.

Pharmacy Phun Phacts

April showers bring May flowers, but what do May flowers bring? Medicine!!!

By: Sarah Witkowski, PharmD, PGY1 Pharmacy Resident

In times past, patients would travel to pick up their medications at a local apothecary who had jars of simples, or the individual botanical, animal, or mineral components which were used to create early compounded medications. Today we have isolated and purified many of the active compounds, but their botanical origins still exist in fields, gardens and flower beds all around us. Here are various examples of common flowers some of our modern medicines and herbal supplements originate from.

Flower: Autumn Crocus (*Cholchium autumnale*)
Medication: Colchicine used to treat gout

Flower: Poppy (*Papaver somniferum*)
Medication: Opium, Morphine, and Codeine used to treat pain

Flower: Madagascar Periwinkle (*Catharanthus species*)
Medication: chemotherapeutic agents Vincristine & Vinblastine

Flower: Purple Cone Flower (*Echinacea purpurea*)
Herbal Supplement: boost immune system/ treat common cold

Flower: Foxglove (*Digitalis purpurea*)
Medication: Digoxin used for heart failure and arrhythmias

Flower: Evening Primrose (*Oenothera biennis*)
Herbal Supplement: skin conditions and metabolic disorders

Yellow Sweet Clover (*Melilotus officinalis*)
Medication: warfarin as an anticoagulant

Flower: St. John's Wort (*Hypericum perforatum*)
Herbal Supplement: used primarily for depression